Golden days of British muscle biochemistry: In memoriam S. V. Perry

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OBITUARY

Golden days of British muscle biochemistry

In memoriam S. V. Perry

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As a tribute to S. V. Perry who to our sorrow left us last December 2009, I would like to recount some memories of my Birmingham connection in the sixties of last century. It will be a personal account only touching lightly on science here and there. Science, however, and in particular muscle science, was our close companion through most of the time I spent in Birmingham in and out of Perry's laboratory. When I came across from Switzerland with wife and three children, I met a solid crew of young investigators in the lab including David Hartshorne, Jake Kendrick-Jones and Ian Trayer. I was a MD who felt that medicine, though a noble profession, was rather an empirical enterprise, which did not satisfy my thirst for knowledge. During my years in Birmingham Perry supported me doing a PhD that should provide me with a more solid basis for doing research in the future. Biochemistry was what I aspired to which was, however, not a curriculum in its own right at the University of Basel at the time when I finished medicine. Perry was an admirable biochemist who got the finishing touch during the years with Kenneth Bailey in Cambridge (Perry 1997). In Perry's lab I avidly soaked up all the biochemical technologies new to me. Asking for explanation of every little detail, I occasionally must have gotten on the nerves of my colleagues who looked down a bit on the foreign MD. The boys in the lab called Perry "Prof" while among themselves they talked about "Sam" (Samuel). My relation to "Prof" was a bit of an exception, he told me to address him by "Victor" as he was privately called in his family and by friends. So I did, but always with a certain uncertainty, until years later when our relation grew into a deep friendship. With retrospect this development may have been facilitated by me gaining more self-confidence. However, from my perspective Victor Perry has always remained one of the scientific giants I was privileged to know well (Fig. 1).

In the lab we were messing around with preparations from rabbit muscle chasing for protein factors that inhibited the actomyosin MgATPase and conferred Ca^{2+}-sensitivity to the system. One day we got the activities, the next day they had vanished, we were hardly getting anywhere. In the morning Victor used to ask, with which leg did you first get out of bed today? He strongly held that biochemistry is closely related to gourmet cooking. So we were cooking all day until late in the evening. The proof of the pudding is in the eating, and last Friday of the month we usually got a keg of beer and were all on the booze. Victor mindful of the clean and punctual "Swiss qualities" asked me to look after the boys and keep the lab tidy, a task none too easy to live up to. In exchange, living closest to the Biology Tower of the Birmingham University, on Saturdays and Sundays I went to the lab to change the dialyses, mine and everybody else's. Often I took our 6 years old son who was then at Bournville primary school with me. When in school he had to write a composition on daddy's job, he wrote "my father is a water changer"; he thought I was doing this all week long.

Britain has for decades been a stronghold in muscle research, particularly fostering physiological and structural studies. In the fifties Sam Perry prominently shifted emphasis towards biochemistry by studying the chemical properties of isolated myofibrils and actomyosin (Perry 1956). In the June 2006 issue of "The Biochemist" Prof. Perry was dubbed "one of the founding fathers of muscle biochemistry". At that time the Perry lab was first to confirm that traces of Ca^{2+} are critically regulating

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myofibrillar activity employing the cation chelator glycolcomplexon (Perry and Grey 1956) which was obtained from Gerold Schwarzenbach, Anorganic Chemistry, Swiss Federal Institute of Technology (ETH, Zurich). Glycolcomplexon, later to be known as EGTA, specifically chelates Ca^{2+} ions with an affinity 6 orders of magnitude ($pK_1 = 11$) higher than it binds Mg^{2+} ($pK_1 = 5.2$), thus allowing differentiation of biological function between these two crucial divalent cations in muscle. During my time (late sixties) in Perry's lab the introduction of routine usage of SDS-PAGE in 6 M urea and chromatography on 1–2 m long Sephadex G-200 columns in 6 M guanidine hydrochloride (conditions taken over from Charles Tanford, then at Duke University, USA) led to resolution and characterisation of the different troponin components associated with tropomyosin (Schaub and Perry 1971; Schaub et al. 1972). The Ca^{2+}-regulatory properties were first assigned to the so-called "native" tropomyosin preparation by Setsuro Ebashi (Ebashi 1963). The combined efforts of mainly the three laboratories of Ebashi (Tokyo), Gergely (Boston), and Perry (Birmingham, UK) led in 1972 at the memorable Cold Spring Harbor Symposium on Muscle Contraction (The mechanism of muscle contraction 1973) to a general consensus on function and nomenclature of troponin consisting of three functionally different subunits: TnI (former inhibitory factor or troponin-B), TnC (former Ca^{2+}-sensitizing factor or troponin-A) and TnT (anchoring the troponin components to tropomyosin). What we did not know in the sixties was the unrivalled surge of the cardiac isoforms of both troponin-I and troponin-T in serum immunoassay to achieve worldwide acceptance in clinical medicine as the "gold standard" for evaluation of cardiac infarction in diagnostics and prognostics. In a most recent clinical publication the troponin-test was praised as the top sensitive marker for cardiac damage, even superior to the electrocardiogram (Muehlschlegel et al. 2009).

Fig. 1 Prof. S. V. Perry in official mission at one of the muscle conferences during the seventies

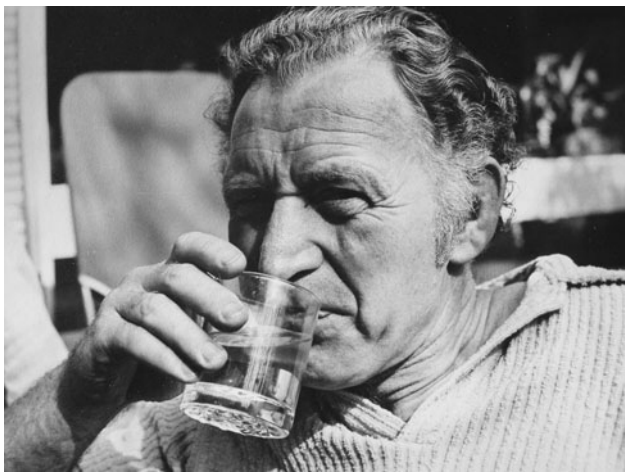

Fig. 2 Sam Perry privately in Zurich (Switzerland) during the seventies

It was a great privilege for me to have been introduced by Victor Perry to biochemistry and the halcyon British way of life, to assist in groundbreaking research on regulation of muscle contraction, to make friends with coworkers in Perry's group (many more stories could be told), to learn to do earnest research, deploring failures and being thrilled when success occurred (though definitely more seldom than failures), but also to enjoy campus life. Occasionally, Victor took me along to the "Muscle Dinners" informally held in turn among the British muscle laboratories (Perry 1997). When 1970 returning back to Switzerland, I missed an equivalent coherence between the muscle research centers on the Continent as was the case in Great Britain. It proved impracticable to hold occasional Muscle Dinners on the much larger scale of whole Europe. Thus, together with a few friends including Caspar Rüegg (Heidelberg, Germany) and the late Gabriel Hamoir (Liege, Belgium) who were quite enthusiastic about, we started the European Muscle Club (EMC), later to be renamed European Society for Muscle Research (ESMR), in order to bring the dispersed muscle laboratories on the Continent closer together and initiate cooperations (Schaub 2008). The ESMR has flourished over the years and in 2010 the 39th Muscle Conference will be held in Padova (Italy) after having been accommodated in the past four times in Britain. I must give credit to Victor for without him the ESMR would never have gone off the ground, Victor inspired the idea and hovered behind the scene as Grey Eminence. The lasting friendship with Victor did not stop me to admire him and looking up to him (Fig. 2).

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